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 s
 . (FILE 'HOME' ENTERED AT 16:42:59 ON 21 AUG 2001)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:43:16 ON 21 AUG 2001
L1         10471 S (ANTIBOD?) (10N) ((GAMMA INTERFERON) OR (INTERFERON GAMMA) OR
L2           558 S L1 (10N) ADMINIST?
L3            12 S L2 (P) ((AIDS) OR (ACQUIRED IMMUNODEFICIENCY DIEASE
L4             4 DUP REM L3 (8 DUPLICATES REMOVED)

=> s (antibod?) (10N) ((alpha interferon) or (interferon alpha) or (IFN alpha) or (alpha IFN))
L5          3815 (ANTIBOD?) (10N) ((ALPHA INTERFERON) OR (INTERFERON ALPHA) OR
                 (IFN ALPHA) OR (ALPHA IFN))

=> s l5 (10N) administ?
L6           103 L5 (10N) ADMINIST?

=> s l6 (P) ((AIDS) or (Acquired Immunodeficiency disease))
L7             0 L6 (P) ((AIDS) OR (ACQUIRED IMMUNODEFICIENCY DISEASE))

=> s (antibod?) (10N) ((TNF alpha) or (TNF?) or (tumor necrosis factor alpha) or (tumor necrosis factor?
   3 FILES SEARCHED...
L8         15929 (ANTIBOD?) (10N) ((TNF ALPHA) OR (TNF?) OR (TUMOR NECROSIS FACTO
                 R ALPHA) OR (TUMOR NECROSIS FACTOR?))

=> s l8 (10N) administ?
L9           851 L8 (10N) ADMINIST?

=>
=> s l9 (P) (AIDS or (acquired immunodeficieny disease))
L10            9 L9 (P) (AIDS OR (ACQUIRED IMMUNODEFICIENY DISEASE))

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11            3 DUP REM L10 (6 DUPLICATES REMOVED)

=> dis l11 1-3 ibib abs kwic

L11  ANSWER 1 OF 3      MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    96074694     MEDLINE
DOCUMENT NUMBER:     96074694   PubMed ID: 7479982
TITLE:               Spontaneous inflammatory demyelinating disease in
                     transgenic mice showing central nervous system-specific
                     expression of tumor necrosis factor alpha.
AUTHOR:              Probert L; Akassoglou K; Pasparakis M; Kontogeorgos G;
                     Kollias G
CORPORATE SOURCE:    Department of Molecular Genetics, Hellenic Pasteur
                     Institutte, Athens, Greece.
SOURCE:              PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE
                     UNITED STATES OF AMERICA, (1995 Nov 21) 92 (24) 11294-8.
                     Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199512
ENTRY DATE:          Entered STN: 19960124
                     Last Updated on STN: 19960124
                     Entered Medline: 19951228
AB   Cytokines are now recognized to play important roles in the physiology of
     the central nervous system (CNS) during health and disease. Tumor necrosis
     factor alpha (TNF-alpha) has been implicated in the pathogenesis of
     several human CNS disorders including multiple sclerosis, AIDS
     dementia, and cerebral malaria. We have generated transgenic mice that
     constitutively express a murine TNF-alpha transgene, under the control of
     its own promoter, specifically in their CNS and that spontaneously develop
     a chronic inflammatory demyelinating disease with 100% penetrance from
     around 3-8 weeks of age. High-level expression of the transgene was seen
     in neurons distributed throughout the brain. Disease is manifested by
     ataxia, seizures, and paresis and leads to early death. Histopathological
     analysis revealed infiltration of the meninges and CNS parenchyma by CD4+
     and CD8+ T lymphocytes, widespread reactive astrocytosis and microgliosis,
     and focal demyelination. The direct action of TNF-alpha in the
     pathogenesis of this disease was confirmed by peripheral
     administration of a neutralizing anti-murine TNF-
     alpha antibody. This treatment completely prevented the
     development of neurological symptoms, T-cell infiltration into the CNS
     parenchyma, astrocytosis, and demyelination, and greatly reduced the
     severity of reactive microgliosis. These results demonstrate that
     overexpression of TNF-alpha in the CNS can cause abnormalities in nervous
     system structure and function. The disease induced in TNF-alpha transgenic
     mice shows clinical and histopathological features characteristic of
     inflammatory demyelinating CNS disorders in humans, and these mice
     represent a relevant in vivo model for their further study.
AB    . . . disease. Tumor necrosis factor alpha (TNF-alpha) has been
     implicated in the pathogenesis of several human CNS disorders including
     multiple sclerosis, AIDS dementia, and cerebral malaria. We have
     generated transgenic mice that constitutively express a murine TNF-alpha
     transgene, under the control of. . .  and microgliosis, and focal
     demyelination. The direct action of TNF-alpha in the pathogenesis of this
     disease was confirmed by peripheral administration of a
     neutralizing anti-murine TNF-alpha antibody.
     This treatment completely prevented the development of neurological
     symptoms, T-cell infiltration into the CNS parenchyma, astrocytosis, and
     demyelination, and greatly. . . .

L11  ANSWER 2 OF 3  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        1995:202391  CAPLUS
DOCUMENT NUMBER          122:7781
TITLE:                   Anti-IL-4 monoclonal antibody and IFN-.gamma.
                         administration retards development of immune
                         dysfunction and cytokine dysregulation during murine
                         AIDS
AUTHOR(S):               Wang, Y.; Ardestani, S. K.; Liang, B.; Beckham, C.;
                         Watson, R. R.
CORPORATE SOURCE:        Department Family Community Medicine, University
                         Arizona, Tucson, AZ, USA
SOURCE:                  Immunology (1994), 83(3), 384-9
                         CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   This study was designed to det. if administration of anti-interleukin-4
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LOGINID:ssspta1644axd
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * *     Welcome to STN International     * * * * * * * * * *

 NEWS  1            Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Jan 25    The CA Lexicon available in the CAPLUS and CA files
 NEWS  3  Feb 06    Engineering Information Encompass files have new names
 NEWS  4  Feb 16    TOXLINE file now being updated
 NEWS  5  Apr 23    Search Derwent WPINDEX by chemical structure
 NEWS  6  Apr 23    PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
 NEWS  7  May 07    DGENE Reload
 NEWS  8  Jun 20    Published patent applications (A1) are now in USPATFULL
 NEWS  9  JUL 13    New SDI alert frequency now available in Derwent's
                    DWPI and DPCI

 NEWS EXPRESS  August 15 CURRENT WINDOWS VERSION IS V6.0c,
               CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
               AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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FILE 'HOME' ENTERED AT 14:42:58 ON 21 AUG 2001

=> file medline caplus embase biosis
COST IN U.S. DOLLARS                               SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                      0.15       0.15

FILE 'MEDLINE' ENTERED AT 14:43:16 ON 21 AUG 2001

FILE 'CAPLUS' ENTERED AT 14:43:16 ON 21 AUG 2001
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=> s antibod? (L) (IFN-gamma or gamma interferon or interferon gamma or IFN gamma or gamma IFN)
L1        17471 ANTIBOD? (L) (IFN-GAMMA OR GAMMA INTERFERON OR INTERFERON GAMMA OR
                IFN GAMMA OR GAMMA IFN)

=> s l1 (L)N administ?
L2          158 L1 (L)N ADMINIST?

=> s l2 and (AIDS or (acquired immunodeficiency disease)
UNMATCHED LEFT PARENTHESIS 'AND (AIDS'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l2 and (AIDS or (acquired immunodeficiency disease))
L3           11 L2 AND (AIDS OR ACQUIRED IMMUNODEFICIENCY DISEASE)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4            4 DUP REM L3 (7 DUPLICATES REMOVED)

=> d l4 1-4 ibib abs total

L4   ANSWER 1 OF 4     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:          [illegible]     MEDLINE
DOCUMENT NUMBER:       [illegible]    PubMed ID: [illegible]
TITLE:                 Protection against lethal toxoplasmosis in mice by an
                       avirulent strain of Toxoplasma gondii: stimulation of
                       IFN-gamma and TNF-alpha response.
AUTHOR:                Haque S; Franck J; Dumon H; Kasper L H; Haque A
CORPORATE SOURCE:      Department of Medicine and Microbiology, Dartmouth Medical
                       School, Hanover, New Hampshire, 03755, USA.
                       [illegible]
SOURCE:                EXPERIMENTAL PARASITOLOGY, (1999 Dec) [illegible].
                       Journal code: [illegible]. ISSN: 0014-4894.
PUB. COUNTRY:          United States
                       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:              English
FILE SEGMENT:          Priority Journals
ENTRY MONTH:           [illegible]
ENTRY DATE:            Entered STN: [illegible]
                       Last Updated on STN: [illegible]
                       Entered Medline: [illegible]
AB   In this study, we examined whether the [illegible] could be used for [illegible]
     AIDS [illegible]
     [illegible]
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     immune system early in infection since they produced higher levels of
     IFN-gamma, TNF-alpha, and NO than FIP-infected mice.
     Administration of anti-IFN-gamma mAb or
     anti-asialo GM1 antibody resulted in [illegible] and [illegible] mortality,
     respectively, in FIN-infected mice but not [illegible] death in FIN + FIP-infected
     mice. Together, these results suggest that early production of IFN-gamma
     and NK-cell activity is important in protection against FIN infection,
     whereas in FIN + FIP infection, components of adaptive immunity rapidly
     developed following elimination of an effective early innate immune
     response.
     Copyright 1999 Academic Press.
AB   In this study, we examined whether the FIN strain, isolated from an
     AIDS patient [illegible]
     in mice against infection with a lethal dose of the FIP strain. Mice [illegible]
     activate the immune system early in infection since they produced
     higher levels of IFN-gamma, TNF-alpha, and NO than FIP-infected mice.
     Administration of anti-IFN-gamma mAb or
     anti-asialo GM1 antibody resulted in [illegible] mortality,
     respectively, in FIN-infected mice but not [illegible] death in FIN + FIP-infected
     mice. Together, these. . .

L4   ANSWER 2 OF 4      MEDLINE                          DUPLICATE 2
ACCESSION NUMBER:    [illegible]      MEDLINE
DOCUMENT NUMBER:     [illegible]   PubMed ID: [illegible]
TITLE:               T cells cooperate with passive antibody to modify
                     Cryptococcus neoformans infection in mice.
AUTHOR:              Yuan R R; Casadevall A; Oh J; Scharff M D
CORPORATE SOURCE:    Department of Cell Biology, Albert Einstein College of
                     Medicine, Bronx, NY 10461, USA.
CONTRACT NUMBER:     AI-33142 (NIAID)
                     AI-33774 (NIAID)
                     P30 CA-13330 (NCI)
SOURCE:              PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE
                     UNITED STATES OF AMERICA, (1997 Mar 18) 94 (6) 2483-8.
                     Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199704
ENTRY DATE:          Entered STN: [illegible]
                     Last Updated on STN: [illegible]
                     Entered Medline: [illegible]
AB   Cryptococcus neoformans is an encapsulated fungus that is a major cause of
     meningitis in patients with AIDS. In immunocompetent mice,
     administration of IgG1 mAb protects against cryptococcal infection,
     whereas administration of IgG3 is not protective and can accelerate the
     infection. In beige mice with impaired natural killer cell function, the
     effects of IgG1 and IgG3 are similar to those observed in immunocompetent
     mice, suggesting that natural killer cells are not crucial for
     antibody-mediated regulation of cryptococcal infection. In mice lacking
     CD4+ T cells, IgG1 is not protective and IgG3 accelerates infection,
     indicating that CD4+ T cells are required for antibody-mediated
     protection. In mice lacking CD8+ T cells, both IgG1 and IgG3 antibodies
     prolong survival, indicating that acceleration of the disease process by
     IgG3 involves CD8+ T cells. Both IgG1-mediated protection and
     IgG3-mediated acceleration of infection require interferon
     gamma. These results reveal a functional dependence of passively
     administered antibody on cellular immunity in
     cryptococcal infection in mice and have implications for antibody-based
     therapies in humans in the setting of CD4+ lymphopenia.
AB   Cryptococcus neoformans is an encapsulated fungus that is a major cause of
     meningitis in patients with AIDS. In immunocompetent mice,
     administration of IgG1 mAb protects against cryptococcal infection,
     whereas administration of IgG3 is not protective and can. . .
     acceleration of the disease process by IgG3 involves CD8+ T cells. Both
     IgG1-mediated protection and IgG3-mediated acceleration of infection
     require interferon gamma. These results reveal a
     functional dependence of passively administered antibody
     on cellular immunity in cryptococcal infection in mice and have
     implications for antibody-based therapies in humans in the setting of. . .


L4   ANSWER 3 OF 4      MEDLINE                          DUPLICATE 3
ACCESSION NUMBER:    [illegible]      MEDLINE
DOCUMENT NUMBER:     [illegible]   PubMed ID: [illegible]
TITLE:               Anti-IL-4 monoclonal antibody and IFN-
                     gamma administration retards development
                     of immune dysfunction and cytokine dysregulation during
                     murine AIDS.
AUTHOR:              Wang Y; Ardestani S K; Liang B; Beckham C; Watson R R
CORPORATE SOURCE:    Department of Family and Community Medicine, University of
                     Arizona, Tucson 85724.
CONTRACT NUMBER:     [illegible]
SOURCE:              IMMUNOLOGY, (1994 Nov) 83 (3) 384-9.
                     Journal code: [illegible] ISSN: [illegible]
PUB. COUNTRY:        ENGLAND: United Kingdom
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         [illegible]
ENTRY DATE:          Entered STN: [illegible]
                     Last Updated on STN: [illegible]
                     Entered Medline: [illegible]
AB   [illegible] administration of
     anti-interleukin-4 (IL-4) monoclonal antibody (mAb) and
     interferon gamma (IFN-gamma) [illegible]
     [illegible]
     [illegible] AIDS [illegible]
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into the roles of immunomodulation in **AIDS** treatment as well as the mechanisms by which retrovirus infection induces cytokine dysregulation, facilitating immunodeficiencies in **AIDS**.

TI Anti-IL-4 monoclonal **antibody** and **IFN-gamma** **administration** retards development of immune dysfunction and cytokine dysregulation during murine **AIDS**.

AB This study was designed to determine if **administration** of anti-interleukin-4 (IL-4) monoclonal **antibody** (mAb), **interferon-gamma** (**IFN-gamma**) and their combination after LP-BM5 retrovirus infection of female C57BL/6 mice would prevent retrovirus-induced immunosuppression and cytokine dysregulation. [illegible] IL-2 and IFN-gamma release by splenocytes, and alleviated splenomegaly and hypergammaglobulinemia, precursor signs of development of acquired immune deficiency syndrome (**AIDS**). These findings could provide insight into the roles of immunomodulation in **AIDS** treatment as well as the mechanisms by which retrovirus infection induces cytokine dysregulation, facilitating immunodeficiencies in **AIDS**.

L4 ANSWER 4 OF 4 EMBASE COPYRIGHT [illegible] ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94[illegible] EMBASE
DOCUMENT NUMBER: 1994[illegible]
TITLE: Biological response modifiers and parasitic infections: Experimental aspects of toxoplasmosis.
AUTHOR: Beaman M.H.
CORPORATE SOURCE: University Department of Medicine, Fremantle Hospital, P.O. Box 480, Fremantle, WA 6160, Australia
SOURCE: Canadian Journal of Infectious Diseases, (1994) 5/SUPPL. A (4A-7A).
ISSN: 1180-2332 CODEN: [illegible]
COUNTRY: Canada
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; French

AB Parasitic infections are important causes of disease in the developing world and, since the advent of **AIDS**, the developed world. Over the past decade, in vitro and in vivo studies have established the important role that biological response modifiers play in pathogenesis of parasitic disease. These basic studies have resulted in successful clinical trials of interferon gamma (IFN-.gamma.) in human leishmaniasis. Toxoplasmic encephalitis is a major opportunistic infection in patients with **AIDS**, and current therapy is often problematic. IFN-.gamma. has been shown in in vitro and in vivo animal studies to be critical for host defence against Toxoplasma gondii. Tumour necrosis factor alpha plays a critical role in mediating IFN-.gamma. effect in vitro, but its role in vivo is under further study. Interleukin (IL)-6 and IL-10 have both recently been shown to enhance T gondii replication in vitro and to antagonize the beneficial effects of IFN-.gamma.. In addition, in certain mouse strains, IL-6 has been shown to worsen mortality from T gondii infection. Future strategies for therapy of T gondii may include **administration** of exogenous **IFN-.gamma.** or IL-12 with or without **antibody** to antagonistic cytokines such as IL-6 or possibly IL-10.

AB Parasitic infections are important causes of disease in the developing world and, since the advent of **AIDS**, the developed world. Over the past decade, in vitro and in vivo studies have established the important role that biological . . . successful clinical trials of interferon gamma (IFN-.gamma.) in human leishmaniasis. Toxoplasmic encephalitis is a major opportunistic infection in patients with **AIDS**, and current therapy is often problematic. IFN-.gamma. has been shown in in vitro and in vivo animal studies to be. . . IL-6 has been shown to worsen mortality from T gondii infection. Future strategies for therapy of T gondii may include **administration** of exogenous **IFN-.gamma.** or IL-12 with or without **antibody** to antagonistic cytokines such as IL-6 or possibly IL-10.

```
=> [illegible]

     (FILE 'HOME' ENTERED AT [illegible] ON [illegible])

     FILE 'MEDLINE, AIDSLINE, EMBASE, BIOSIS' ENTERED AT [illegible] ON [illegible]
L1         [illegible] S ANTIB? (3A) (GAMMA INTERFERON OR INTERFERON GAMMA OR
L2            [illegible] S L1 (L) ADMINIST?
L3              [illegible] S L2 AND (AIDS OR ACQUIRED IMMUNODEFICIENCY DISEASE)
L4              [illegible] DUP REM L3 ([illegible] DUPLICATES REMOVED)

=> s antib? (3a) (alpha interferon or interferon alpha or IFN alpha or alpha IFN)
L5         [illegible] ANTIB? (3A) (ALPHA INTERFERON OR INTERFERON ALPHA OR
                 IFN ALPHA OR ALPHA IFN)

=> s L5 (L) administ?
L6            [illegible] L5 (L) ADMINIST?

=> s L6 and (AIDS or acquired immune deficiency disease)
L7                  L6 AND (AIDS OR ACQUIRED IMMUNODEFICIENCY DISEASE)

=> s antib? (3a) (TNF alpha or (TNF) or tumor necrosis factor alpha or tumor necrosis factor
   or [illegible])
L8        [illegible] ANTIB? (3A) (TNF ALPHA OR TNF OR TUMOR NECROSIS FACT
                 OR ALPHA OR TUMOR NECROSIS FACTOR)

=> s L8 (L) administ?
L9            [illegible] L8 (L) ADMINIST?

=> s L9 and (AIDS or acquired immune deficiency disease)
L10             [illegible] L9 AND (AIDS OR ACQUIRED IMMUNODEFICIENCY DISEASE)

=> dup rem L10
PROCESSING COMPLETED FOR L10
L11              3 DUP REM L10 (1 DUPLICATES REMOVED)

=> d [illegible] L11 1-3 [illegible]

L11  ANSWER 1 OF 3     MEDLINE                                 DUPLICATE 1
ACCESSION NUMBER:    96074634     MEDLINE
DOCUMENT NUMBER:     96074634   PubMed ID: 7479982
TITLE:               Spontaneous inflammatory demyelinating disease in
                     transgenic mice showing central nervous system-specific
                     expression of tumor necrosis factor alpha.
AUTHOR:              Probert L; Akassoglou K; Pasparakis M; Kontogeorgos G;
                     Kollias G
CORPORATE SOURCE:    Department of Molecular Genetics, Hellenic Pasteur
                     Institute, Athens, Greece.
SOURCE:              PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE
                     UNITED STATES OF AMERICA, (1995 Nov 21) 92 (24) 11294-8.
                     Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199601
ENTRY DATE:          Entered STN: 19960124
                     Last Updated on STN: 19960124
                     Entered Medline: 19960122
AB    Cytokines are now recognized to play important roles in the physiology of
      the central nervous system (CNS) during health and disease. Tumor necrosis
      factor alpha (TNF-alpha) has been implicated in the pathogenesis of
      several human CNS disorders including multiple sclerosis, AIDS
      dementia, and cerebral malaria. We have generated transgenic mice that
      constitutively express a murine TNF-alpha transgene, under the control of
      its own promoter, specifically in their CNS and that spontaneously develop
      a chronic inflammatory demyelinating disease with 100% penetrance from
      around 3-8 weeks of age. High-level expression of the transgene was seen
      in neurons distributed throughout the brain. Disease is manifested by
      ataxia, seizures, and paresis and leads to early death. Histopathological
      analysis revealed infiltration of the meninges and CNS parenchyma by CD4+
      and CD8+ T lymphocytes, widespread reactive astrocytosis and microgliosis,
      and focal demyelination. The direct action of TNF-alpha in the
      pathogenesis of this disease was confirmed by peripheral
      administration of a neutralizing anti-murine TNF-
      alpha antibody. This treatment completely prevented the
      development of neurological symptoms, T-cell infiltration into the CNS
      parenchyma, astrocytosis, and demyelination, and greatly reduced the
      severity of reactive microgliosis. These results demonstrate that
      overexpression of TNF-alpha in the CNS can cause abnormalities in nervous
      system structure and function. The disease induced in TNF-alpha transgenic
      mice shows clinical and histopathological features characteristic of
      inflammatory demyelinating CNS disorders in humans, and these mice
      represent a relevant in vivo model for their further study.
AB    . . . disease. Tumor necrosis factor alpha (TNF-alpha) has been
      implicated in the pathogenesis of several human CNS disorders including
      multiple sclerosis, AIDS dementia, and cerebral malaria. We have
      generated transgenic mice that constitutively express a murine TNF-alpha
      transgene, under the control . . . and microgliosis, and focal
      demyelination. The direct action of TNF-alpha in the pathogenesis of this
      disease was confirmed by peripheral administration of a
      neutralizing anti-murine TNF-alpha antibody.
      This treatment completely prevented the development of neurological
      symptoms, T-cell infiltration into the CNS parenchyma, astrocytosis, and
      demyelination, and greatly . . .

L11  ANSWER 2 OF 3     AIDSLINE  [illegible]
ACCESSION NUMBER:        [illegible]     AIDSLINE
DOCUMENT NUMBER:         [illegible]
TITLE:                   Anti-CD4 [illegible] IFN [illegible]
                         [illegible]
                         [illegible]
                         AIDS
AUTHOR:                  [illegible]
                         [illegible]
CORPORATE SOURCE:        [illegible]
                         [illegible]
SOURCE:                  [illegible]
                         [illegible]
DOCUMENT TYPE:           [illegible]
LANGUAGE:                [illegible]
AB   [illegible]
```

IL-4 monoclonal antibody (mAb), interferon-gamma (IFN-gamma) and
their combination after LP-BM5 retrovirus infection of female C57BL/6 mice
would prevent retrovirus-induced immunosuppression and cytokine
dysregulation. Splenic natural killer (NK) cell activity, T- and B-cell
proliferation, and T-helper type 1 (Th1) and Th2 cytokines (IL-2,
IFN-gamma, IL-4 and IL-6) and monokines (IL-6 and tumor necrosis
factor-alpha (TNF-alpha)) secretion were monitored, as they are
usually altered dramatically after murine retrovirus infection.
Administration of IFN-gamma and anti-IL-4 significantly prevented
retrovirus-induced suppression of splenic NK cell activity, and splenic T-
and B-cell proliferation. They also significantly slowed
retrovirus-induced elevation of Th2 cytokine (IL-4 and IL-6) release and
monokine (IL-6 and TNF-alpha) secretion by splenocytes. They prevented
the loss of Th1 cytokine (IL-2 and IFN-gamma) release by splenocytes,
and alleviated splenomegaly and hypergammaglobulinemia, [illegible]
development of acquired immune deficiency syndrome (AIDS). These findings
could provide insight into the roles of immunomodulation in AIDS treatment
as well as the mechanisms by which retrovirus infection induces cytokine
dysregulation, facilitating immunodeficiencies in AIDS.

IT Lymphokines and cytokines
RL: ADV (Adverse effect, including toxicity); MFM (Metabolic formation);
BIOL (Biological study); FORM (Formation, nonpreparative)
(**tumor necrosis factor-.alpha.**,
anti-interleukin 4 monoclonal **antibody** and IFN-.gamma.
administration in murine **AIDS** effect on formation of)

L11 ANSWER [illegible] OF [illegible] MEDLINE DUPLICATE [illegible]
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: Tumor necrosis factor-independent protective effect of
recombinant IFN-gamma against acute toxoplasmosis in T
cell-deficient mice.
AUTHOR: Suzuki Y; [illegible]; Kobayashi A
CORPORATE SOURCE: Department of Parasitology, Teikyo University School of
Medicine, Tokyo, Japan.
SOURCE: JOURNAL OF IMMUNOLOGY, (199[illegible] Oct 1[illegible]) 14[illegible] ([illegible]) 27[illegible]-3[illegible].
Journal code: IFB; [illegible]. ISSN: [illegible].
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 19[illegible]
ENTRY DATE: Entered STN: 19[illegible]
Last Updated on STN: 19[illegible]
Entered Medline: 19[illegible]

AB rIFN-gamma conferred remarkable resistance against acute infection with
Toxoplasma gondii in T cell-deficient (athymic nude) mice. Mice that
received an i.p. injection of rIFN-gamma every other day beginning 24 h
before infection for a total of eight doses survived significantly longer
than untreated control mice although all of the treated mice died after
the lymphokine was discontinued. Mice that received 14 doses of rIFN-gamma
survived significantly longer than those that received eight doses of the
lymphokine although mice started dying soon after the final (14th)
injection of rIFN-gamma and eventually all of the treated mice died.
Histologic study revealed that the IFN-gamma treatment prevented
proliferation of the organisms in all organs examined, including brain,
lung, heart, liver, and spleen. The treatment was effective even when
started 1 day after infection. Peritoneal macrophages obtained from mice
injected with rIFN-gamma were activated and effectively killed tachyzoites
of T. gondii in vitro. TNF activity could not be detected in sera of the
infected mice during treatment with rIFN-gamma. **Administration**
of anti-**TNF antibody** did not affect the protective
effect of rIFN-gamma against T. gondii infection. These facts indicate
that rIFN-gamma can confer resistance to acute infection with T. gondii
without collaboration of lymphokines derived from T cells and TNF. This
suggests that rIFN-gamma may be effective for therapy of toxoplasmosis in
immunosuppressed patients who have impaired activity of T cell function,
especially those with **AIDS**.

AB . . . T. gondii in vitro. TNF activity could not be detected in sera of
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of anti-**TNF antibody** did not affect the protective
effect of rIFN-gamma against T. gondii infection. These facts indicate
that rIFN-gamma can confer resistance. . . . be effective for therapy of
toxoplasmosis in immunosuppressed patients who have impaired activity of T
cell function, especially those with **AIDS**.

=> [illegible]

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     FILE 'HOME' ENTERED AT [illegible] ON [illegible]

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT [illegible] ON [illegible]
L1        [illegible] ANTIB[illegible] (3N) (GAMMA INTERFERON OR INTERFERON GAMMA OR
L2             [illegible] (3N) ADMINIST?
L3             [illegible] AND (AIDS OR ACQUIRED IMMUN? DEFICIENCY DISEASE)
L4              [illegible] DUP REM [illegible] (DUPLICATES REMOVED)
L5           [illegible] ANTIB[illegible] (3N) (ALPHA INTERFERON OR INTERFERON ALPHA OR
L6           [illegible] (3N) ADMINIST?
L7               [illegible] AND (AIDS OR ACQUIRED IMMUNE DEFICIENCY DISEASE)
L8         [illegible] ANTIB[illegible] (3N) (TNF ALPHA OR TNF OR TUMOR NECROSIS FA
L9           [illegible] (3N) ADMINIST?
L10             [illegible] AND (AIDS OR ACQUIRED IMMUNE DEFICIENCY DISEASE)
L11             [illegible] DUP REM [illegible] (DUPLICATES REMOVED)

=> s [illegible] AND (AIDS or Acquired Immune Deficiency Disease)
L12            [illegible] AND (AIDS OR ACQUIRED IMMUNE DEFICIENCY DISEASE)

=> s antib? (3N) interferon (3N) acid labile
L13          [illegible] ANTIB? (3N) INTERFERON (3N) ACID LABILE

=> s L13 [illegible] (AIDS or acquired immune deficiency disease)
L13 NOT FOUND
The L-number entered could not be found. To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s L13 and (AIDS or acquired immune deficiency disease)
L14           [illegible] L13 AND (AIDS OR ACQUIRED IMMUNE DEFICIENCY DISEASE)

=> dup rem L14
PROCESSING COMPLETED FOR L14
L15            1 DUP REM L14 (2 DUPLICATES REMOVED)

=> dis L15 ibib abs kwic

L15  ANSWER 1 OF 1     MEDLINE                               DUPLICATE 1
ACCESSION NUMBER:    [illegible]     MEDLINE
DOCUMENT NUMBER:     [illegible]   PubMed ID: [illegible]
TITLE:               Serum interferon and clinical manifestations of infection
                     with human T-lymphotropic virus type III.
AUTHOR:              [illegible]
SOURCE:              MEDICAL MICROBIOLOGY AND IMMUNOLOGY, [illegible]
                       Journal code: [illegible]. ISSN: [illegible].
PUB. COUNTRY:        GERMANY, WEST: Germany, Federal Republic of
                       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         [illegible]
ENTRY DATE:          Entered STN: [illegible]
                     Last Updated on STN: [illegible]
                     Entered Medline: [illegible]
AB    Sera from [illegible] homosexual men were studied for the presence of
      antibodies against human T-lymphotropic virus type III (HTLV III)
      and acid-labile interferon (IFN) alpha.
      Infection with HTLV III was found to be associated with the presence of
      serum IFN. IFN was detected in [illegible] of sera from male homosexuals with HTLV
      III antibody, but in only [illegible] of sera from antibody-negative individuals.
      More than [illegible] of sera from HTLV III-infected patients with the acquired
      immune deficiency syndrome (AIDS) or pre-AIDS
      conditions (generalized lymphadenopathy or the AIDS-related
      complex) were positive for IFN, while IFN was not present in sera from
      healthy homosexual men with HTLV III antibody. In conclusion, the presence
      of serum IFN may be predictive of the development of AIDS or
      pre-AIDS conditions in male homosexuals exposed to HTLV III.
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      antibodies against human T-lymphotropic virus type III (HTLV III)
      and acid-labile interferon (IFN) alpha.
      Infection with HTLV III was found to be associated with the presence of
      serum IFN. IFN was detected [illegible] of sera from antibody-negative
      individuals. More than [illegible] of sera from HTLV III-infected patients with
      the acquired immune deficiency syndrome (AIDS) or pre-
      AIDS conditions (generalized lymphadenopathy or the AIDS
      -related complex) were positive for IFN, while IFN was not present in sera
      from healthy homosexual men with HTLV III antibody. In conclusion, the
      presence of serum IFN may be predictive of the development of AIDS
      or pre-AIDS conditions in male homosexuals exposed to HTLV III.


=> dis his

     FILE 'HOME' ENTERED AT [illegible] ON [illegible]

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT [illegible] ON [illegible]
L1        [illegible] ANTIB[illegible] (3N) (GAMMA INTERFERON OR INTERFERON GAMMA OR
L2             [illegible] (3N) ADMINIST?
L3             [illegible] AND (AIDS OR ACQUIRED IMMUN? DEFICIENCY DISEASE)
L4              [illegible] DUP REM [illegible] (DUPLICATES REMOVED)
L5          [illegible] ANTIB[illegible] (3N) (ALPHA INTERFERON OR INTERFERON ALPHA OR
L6           [illegible] (3N) ADMINIST?
L7               [illegible] AND (AIDS OR ACQUIRED IMMUNE DEFICIENCY DISEASE)
L8        [illegible] ANTIB[illegible] (3N) (TNF ALPHA OR TNF OR TUMOR NECROSIS FA
L9           [illegible] (3N) ADMINIST?
L10             [illegible] AND (AIDS OR ACQUIRED IMMUNE DEFICIENCY DISEASE)
L11             [illegible] DUP REM [illegible] (DUPLICATES REMOVED)
L12             [illegible] AND (AIDS OR ACQUIRED IMMUNE DEFICIENCY DISEASE)
L13          [illegible] ANTIB? (3N) INTERFERON (3N) ACID LABILE
L14             [illegible] AND (AIDS OR ACQUIRED IMMUNE DEFICIENCY DISEASE)
L15             1 DUP REM L14 (2 DUPLICATES REMOVED)

=> log y
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
[illegible]
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                 [illegible]  [illegible]

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                 [illegible]  [illegible]

STN INTERNATIONAL LOGOFF AT [illegible] ON [illegible]
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=> [illegible]

     FILE '[illegible]' ENTERED AT [illegible] ON [illegible]

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT [illegible] ON [illegible]
L1        [illegible] ANTIBOD? (L) (IFN (W) GAMMA INTERFERON OR INTERFERON GAMMA OR [illegible]
L2          [illegible] L1 (L) IN? ADMINIST?
L3            [illegible] L2 (L) (AIDS OR ACQUIRED IMMUNODEFICIENCY DISEASE)
L4              [illegible] DUP REM L3 ([illegible] DUPLICATES REMOVED)

=> s antibod? (L) (IFN (W) alpha interferon or interferon alpha or IFN alpha or alpha IFN)
L5         [illegible] ANTIBOD? (L) (IFN (W) ALPHA INTERFERON OR INTERFERON ALPHA OR
                  IFN ALPHA OR ALPHA IFN)

=> s l5 (L) in? administ?
L6           [illegible] L5 (L) IN? ADMINIST?

=> s l6 (L) (AIDS or Acquired Immunodeficiency Disease)
L7                [illegible] L6 (L) (AIDS OR ACQUIRED IMMUNODEFICIENCY DISEASE)

=> s antibod? (L) (TNF alpha or TNF[illegible] or tumor necrosis factor alpha or tumor necrosis factor
   [illegible])
L8        [illegible] ANTIBOD? (L) (TNF ALPHA OR TNF[illegible] OR TUMOR NECROSIS FACT
                 OR ALPHA OR TUMOR NECROSIS FACTOR)

=> s l8 (L) in? administ?
L9            [illegible] L8 (L) IN? ADMINIST?

=>
=> s l9 (L) (AIDS or acquired immun? deficiency disease)
L10            [illegible] L9 (L) (AIDS OR ACQUIRED IMMUNODEFICIENCY DISEASE)

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11             3 DUP REM L10 ([illegible] DUPLICATES REMOVED)

=> d l11 1-3 ibib abs kwic

L11  ANSWER 1 OF 3     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    9[illegible]14694     MEDLINE
DOCUMENT NUMBER:     9[illegible]14694   PubMed ID: [illegible]
TITLE:               Spontaneous inflammatory demyelinating disease in
                     transgenic mice showing central nervous system-specific
                     expression of tumor necrosis factor alpha.
AUTHOR:              Probert L; Akassoglou K; Pasparakis M; Kontogeorgos G;
                     Kollias G
CORPORATE SOURCE:    Department of Molecular Genetics, Hellenic Pasteur
                     Institute, Athens, Greece.
SOURCE:              PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE
                     UNITED STATES OF AMERICA, (1995 Nov 21) 92 (24) 11294-8.
                     Journal code: [illegible]. ISSN: [illegible]-8424.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199[illegible]
ENTRY DATE:          Entered STN: 199[illegible]
                     Last Updated on STN: 199[illegible]
                     Entered Medline: 199[illegible]
AB   Cytokines are now recognized to play important roles in the physiology of
     the central nervous system (CNS) during health and disease. Tumor necrosis
     factor alpha (TNF-alpha) has been implicated in the pathogenesis of
     several human CNS disorders including multiple sclerosis, AIDS
     dementia, and cerebral malaria. We have generated transgenic mice that
     constitutively express a murine TNF-alpha transgene, under the control of
     its own promoter, specifically in their CNS and that spontaneously develop
     a chronic inflammatory demyelinating disease with [illegible] penetrance from
     around [illegible] weeks of age. High-level expression of the transgene was seen
     in neurons distributed throughout the brain. Disease is manifested by
     ataxia, seizures, and paresis and leads to early death. Histopathological
     analysis revealed infiltration of the meninges and CNS parenchyma by CD4+
     and CD8+ T lymphocytes, widespread reactive astrocytosis and microgliosis,
     and focal demyelination. The direct action of TNF-alpha in the
     pathogenesis of this disease was confirmed by peripheral
     administration of a neutralizing anti-murine TNF-
     alpha antibody. This treatment completely prevented the
     development of neurological symptoms, T-cell infiltration into the CNS
     parenchyma, astrocytosis, and demyelination, and greatly reduced the
     severity of reactive microgliosis. These results demonstrate that
     overexpression of TNF-alpha in the CNS can cause abnormalities in nervous
     system structure and function. The disease induced in TNF-alpha transgenic
     mice shows clinical and histopathological features characteristic of
     inflammatory demyelinating CNS disorders in humans, and these mice
     represent a relevant in vivo model for their further study.
AB   [illegible] disease. Tumor necrosis factor alpha (TNF-alpha) has been
     implicated in the pathogenesis of several human CNS disorders including
     multiple sclerosis, AIDS dementia, and cerebral malaria. We have
     generated transgenic mice that constitutively express a murine TNF-alpha
     transgene, under the control [illegible] and microgliosis, and focal
     demyelination. The direct action of TNF-alpha in the pathogenesis of this
     disease was confirmed by peripheral administration of a
     neutralizing anti-murine TNF-alpha antibody.
     This treatment completely prevented the development of neurological
     symptoms, T-cell infiltration into the CNS parenchyma, astrocytosis, and
     demyelination, and greatly [illegible]

L11  ANSWER [illegible]
ACCESSION NUMBER:          [illegible]
DOCUMENT NUMBER:           [illegible]
TITLE:                     Anti-[illegible] IFN-gamma[illegible]
                           [illegible]
                           [illegible]
                           AIDS
AUTHOR(S):                 [illegible]
                           [illegible]
CORPORATE SOURCE:          [illegible]
                           [illegible]
SOURCE:                    [illegible]
                           [illegible]
DOCUMENT TYPE:             [illegible]
LANGUAGE:                  English
AB   [illegible]
```

IL-4 monoclonal antibody (mAb), interferon-gamma (IFN-gamma), and
their combination after LP-BM5 retrovirus infection of female C57BL/6 mice
would prevent retrovirus-induced immunosuppression and cytokine
dysregulation. Retrovirus suppressed natural killer (NK) cell activity, T- and B-cell
proliferation, and T-helper type 1 (Th1) and Th1 cytokines (IL-2,
IFN-gamma), [illegible] and IL-[illegible] and monokine (IL-6 and tumor necrosis
factor-alpha (TNF-alpha)). [illegible] were [illegible]
[illegible] dramatically after murine retrovirus infection.
Administration of IFN-gamma and anti-IL-4 significantly prevented
retrovirus-induced suppression of splenic NK cell activity, and splenic T-
and B-cell proliferation. They also significantly slowed
retrovirus-induced elevation of Th2 cytokine (IL-5 and IL-10) release and
monokine (IL-6 and TNF-alpha) secretion by splenocytes. They prevented
the loss of Th1 cytokine (IL-2 and IFN-gamma) release by splenocytes,
and alleviated splenomegaly and hypergammaglobulinemia, products of murine
development of acquired immune deficiency syndrome (AIDS). These findings
could provide insight into the roles of immunomodulation in AIDS treatment
as well as the mechanisms by which retrovirus infection induces cytokine
dysregulation, facilitating immune deficiencies in AIDS.

IT Lymphokines and Cytokines
RL: ADV (Adverse effect, including toxicity); MFM (Metabolic formation);
BIOL (Biological study); FORM (Formation, nonpreparative)
tumor necrosis factor-.alpha.,
anti-interleukin 4 monoclonal **antibody** and IFN-.gamma.
administration in murine **AIDS** effect on formation

L11 ANSWER 4 OF 4 MEDLINE DUPLICATE 2
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible]
TITLE: Tumor necrosis factor-independent protective effect of
recombinant IFN-gamma against acute toxoplasmosis in T
cell-deficient mice.
AUTHOR: Suzuki Y; Joh K; Kobayashi A
CORPORATE SOURCE: Department of Parasitology, Jikei University School of
Medicine, Tokyo, Japan.
SOURCE: JOURNAL OF IMMUNOLOGY, (1991 Oct 15) 147 (8) 2728-33.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911115

AB rIFN-gamma conferred remarkable resistance against acute infection with
Toxoplasma gondii in T cell-deficient (athymic nude) mice. Mice that
received an i.p. injection of rIFN-gamma every other day beginning 24 h
before infection for a total of eight doses survived significantly longer
than untreated control mice although all of the treated mice died after
the lymphokine was discontinued. Mice that received 14 doses of rIFN-gamma
survived significantly longer than those that received eight doses of the
lymphokine although mice started dying soon after the final (14th)
injection of rIFN-gamma and eventually all of the treated mice died.
Histologic study revealed that the IFN-gamma treatment prevented
proliferation of the organisms in all organs examined, including brain,
lung, heart, liver, and spleen. The treatment was effective even when
started 1 day after infection. Peritoneal macrophages obtained from mice
injected with rIFN-gamma were activated and effectively killed tachyzoites
of T. gondii in vitro. TNF activity could not be detected in sera of the
infected mice during treatment with rIFN-gamma. **Administration**
of anti-**TNF antibody** did not affect the protective
effect of rIFN-gamma against T. gondii infection. These facts indicate
that rIFN-gamma can confer resistance to acute infection with T. gondii
without collaboration of lymphokines derived from T cells and TNF. This
suggests that rIFN-gamma may be effective for therapy of toxoplasmosis in
immunosuppressed patients who have impaired activity of T cell function,
especially those with **AIDS**.

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effect of rIFN-gamma against T. gondii infection. These facts indicate
that rIFN-gamma can confer resistance. . . . be effective for therapy of
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cell function, especially those with **AIDS**.

=> [illegible]